REMARKS

1. **STATUS OF THE CLAIMS**

Claims 1-31 are pending.

Claims 23-31 have been withdrawn by the Examiner as being directed to a non-elected invention.[1]

Claim withdrawals were made notwithstanding Applicant's belief that the unamended claims would have been allowable, without acquiescing to any of the Examiner's arguments, and without waiving the right to prosecute the unamended (or similar) claims in another application, but rather for the purpose of furthering Applicant's business goals and expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG).[2]

2. **REJECTION OF CLAIMS 1-21 UNDER 35 U.S.C. §102(b) OVER PAPAYANNOPOULOU *et al.* (WO 94/11027)**

The Examiner rejected Claims 1-21 under 35 U.S.C. §102(b) for alleged anticipation by Papayannopoulou *et al.* (WO 94/11027).[3] Applicant respectfully traverses because Papayannopoulou *et al.* does not disclose the limitation that the target tissue is "not bone marrow" endothelial tissue. Under the law,

> "Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration."[4] The corollary to that holding is that "absence from the reference of any claimed element negates anticipation."[5]

Papayannopoulou *et al.* discloses "peripheralizing $CD34^+$ cells, including hematopoietic stem cells . . . by administering a blocking agent of VLA-4 antigen [also known as integrin $\alpha 4\beta 1$]

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1 Office Action, page 2, 3rd paragraph.
2 65 Fed. Reg. 54603 (September 8, 2000).
3 Office Action, page 2, item 4.
4 *W.L. Gore & Assoc., Inc v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303, 313 (Fed. Cir. 1983), cert. denied, 105 S. Ct. 172 (1984), citing *Soundscriber Corp. v. U.S.*, 360 F.2d 954, 960, 148 USPQ 298, 301, adopted, 149 USPQ 640 (Ct. Cl. 1966).
5 *Rowe v. Dror*, 42 USPQ2d 1550, 1553 (Fed. Cir. 1997), citing *Kloster Speedsteel AB v. Crucible, Inc.*, 793 F.2d 1565, 1571, 230 USPQ 81, 84 (Fed. Cir. 1986).

on the surface of $CD34^+$ cells."[6] Papayannopoulou *et al.* discloses that "peripheralization of hematopoietic stem cells" means "increasing the number of hematopoietic stem cells and $CD34^+$ cells in peripheral blood."[7] Papayannopoulou *et al.* also discloses that peripheralization of hematopoietic stem cells offers the advantage of "utilizing peripheral blood as a source for autologous stem cell transplantation"[8] instead of the prior art's use of bone marrow for hematopoietic stem cell transplantation in chemotherapy and radiotherapy.[9] Papayannopoulou *et al.*'s peripheralization is achieved by administering a blocking agent of integrin $\alpha4\beta1$ to hematopoietic stem cells in bone marrow, thereby effecting their release from bone marrow into peripheral blood. In this regard, Papayannopoulou *et al.* explains that

> "Applicant believes that administering a blocking agent of VLA-4 antigens on the surface of hematopoietic stem cells and CD34+ cells causes peripheralization of these cells by mediating release of the cells from the **marrow** environment via disruption of interactions between VLA-4 and its microenvironmental ligands, such as fibronectin and/or VCAM-1 on stromal cells or in the ECM."[10]

It is important to note that Papayannopoulou *et al.*'s methods require administering, to **bone marrow tissue,** agents that alter integrin $\alpha4\beta1$'s binding to its ligand. In contrast, the invention's methods exclude bone marrow endothelial tissue by reciting that the target tissue is "**not bone marrow**" endothelial tissue.

Because Papayannopoulou *et al.* fails to discloses a limitation of the claims, it cannot anticipate. Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection of Claims 1-21 under 35 U.S.C. §102(b) over Papayannopoulou *et al.*

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6 Papayannopoulou *et al.*, Abstract, and page 6, lines 26-33.
7 Papayannopoulou *et al.*, page 6, lines 26-33.
8 Papayannopoulou *et al.*, page 3, lines 30-33. Also, Papayannopoulou *et al.*, page 3, lines 30-32 says that peripheralization means "to release stem cells from the bone marrow environment into the periphery" of blood vessels, "thus increasing the number of stem cells in peripheral blood."
9 Papayannopoulou *et al.*, page 2, lines 25-31.
10 (Emphasis added) Papayannopoulou *et al.*, page 25, lines 1-9.

3. **REJECTION OF CLAIMS 1-21 UNDER 35 U.S.C. §102(e) OVER VARNER (WO 03/019136)**

The Examiner rejected Claims 1-21 under 35 U.S.C. §102(e) for alleged anticipation by Varner (WO 03/019136) (hereafter referred to as '136).[11] Applicant respectfully disagrees because '136 does not disclose at least 3 limitations of the claims, as further explained below.

A. Bone Marrow is a Target Tissue in WO 03/019136

Unlike the instant claims that exclude "bone marrow endothelial tissue," the methods of '136 include administering, to **bone endothelial tissue**, agents that inhibit binding of integrin α4β1 to its ligand. These agents are administered in the methods of '136 for the purpose of reducing angiogenesis in bone,[12] such as angiogenesis that is associated with bone cancer.[13] Thus, '136 does not disclose the limitation of target tissue that is "not bone marrow endothelial tissue."

B. WO 03/019136 does not disclose altering adhesion of hematopoietic progenitor cells

The methods of '136 relate to altering participation of hematopoietic progenitor cells in different phenomena from the recited phenomenon of adhesion. In particular, the methods of '136 employ agents that inhibit binding of integrin **α4β1** to its ligand in order to reduce migration of progenitor endothelial cells,[14] and to prevent the participation of endothelial progenitor cells in

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11 Office Action, page 3, item 5.

12 WO 03/019136 says "In particularly preferred embodiments, the invention provides a method for **inhibiting angiogenesis** in a tissue, comprising: a) providing at least one tissue and an agent which inhibits specific binding of integrin α4β1 to an integrin α4β1 ligand; b) treating the tissue with the agent under conditions such that specific binding of integrin α4β1 to the integrin α4β1 ligand is inhibited and a treated tissue is produced; and c) observing inhibition of angiogenesis in the treated tissue . . . In yet another preferred embodiment, the tissue comprises ocular tissue, skin tissue, **bone tissue**, or synovial tissue." (Emphasis added) WO 03/019136, paragraph bridging pages 3-4. See also, page 5, 2nd paragraph.

13 WO 03/019136 says "In an alternative preferred embodiment, the malignant tumor is. . . **bone cancer** . . ." (Emphasis added) WO 03/019136, page 5, 2nd paragraph.

14 WO 03/019136 says ". . . agents which inhibit the specific binding of integrin α4β1 to one or more of its ligands block the outgrowth of new blood vessels from pre-existing vessels, and/or block the ability of circulating endothelial cells and/or **progenitor endothelial cells** from leaving the bloodstream and entering and **migrating** through tissues to sites of hypoxia or growth factor secretion where they may participate in the formation of new blood vessels." (Emphasis added) WO 03/019136, page 13, 2nd paragraph. See also Example 12 of '132, entitled "Inhibition of Endothelial Progenitor Cell **Migration** in *In Vivo* Mouse and Rat Animal Models." (Emphasis added) WO 03/019136, page 66.

angiogenesis.[15] The '136's phenomena of **migration and angiogenesis** are distinguished from the phenomenon of **"adhesion"** of hematopoietic progenitor cells that is altered by the instantly claimed methods. Therefore, '136 does not disclose the limitation of altering "adhesion" of hematopoietic progenitor cells.

C. WO 03/019136 discloses altering adhesion of mature endothelial cells, not of hematopoietic progenitor cells

The methods of '136 relate to altering adhesion of a cell type (*i.e.*, of mature **endothelial** cells)[16] that is different from the recited **hematopoietic progenitor** cells. Because '136 lacks this limitation, it does not anticipate the claims.

In sum, since '136 lacks not just one, but at least 3 of the claims' limitations, Applicant respectfully requests that the rejection of Claims 1-21 under 35 U.S.C. §102(e) over '136 be withdrawn.

CONCLUSION

Applicants respectfully request reconsideration of the application in view of the above, which places the claims in condition for allowance. To expedite prosecution, Applicants also

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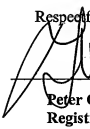
15 See, Example 18 of '132, entitled "Antagonists of integrin α4β1 prevent the participation of endothelial progenitor cells in **angiogenesis.**" (Emphasis added) WO 03/019136, page 69.

16 WO 03/019136 says "Also provided herein are methods for inhibiting **endothelial cell adhesion**, comprising: a) providing endothelial cells and an agent which inhibits specific binding of integrin α4β1 to an integrin α4β1 ligand; b) treating the endothelial cells with the agent under conditions such that specific binding of integrin α4β1 to the integrin α4β1 ligand is inhibited and treated endothelial cells are produced; and c) observing inhibition of cell adhesion of the treated endothelial cells." (Emphasis added) WO 03/019136, page 4, last full paragraph. WO 03/019136 also discloses that "Figure 3 shows inhibition of **endothelial cell adhesion** (A), and **migration** (B) by anti-integrin α4β1 antibody antagonists." (Emphasis added) WO 03/019136, page10, 3rd paragraph. See also WO 03/019136, Example 3, beginning on page 60, entitled "Inhibition of Human Neonatal Cell **Adhesion** to, and Migration of Human Vascular **Endothelial Cells** on, CS-1 Fibronectin by Anti-Integrin α4β1 **Antibody**." Emphasis added.

respectfully invite the Examiner to **call the undersigned before drafting another written communication**, if any.

Respectfully submitted



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